When evidence meets artificial intelligence

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Summary

Evidence-based medicine (EBM) integrates clinical expertise, patient values, and best available research evidence, yet classical trial-based approaches struggle to accommodate the scale, heterogeneity, and structural constraints of contemporary health systems. The rapid expansion of biomedical data is positioning artificial intelligence (AI) as an extension of evidence generation rather than a replacement for epidemiologic reasoning. This state-of-the-art Review examines how AI is beginning to reshape the methodological and ethical foundations of EBM through multimodal data integration, target trial emulation, and simulation-based modelling, while emphasizing that predictive performance does not ensure causal validity or clinical benefit. Implementation depends on rigorous epidemiologic design, integration within clinical informatics systems, and effective human–machine collaboration. In the Americas, fragmented health systems and uneven digital infrastructures constrain representativeness and equitable deployment. AI will not transform EBM on its own; its constructive role requires governance reform, transparent validation, and structural change to prevent the reinforcement of existing inequities.

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Introduction

In 1996, Sackett et al. defined Evidence-Based Medicine (EBM) as "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients"[1] This framework brought together clinical expertise, patient preferences, and empirical evidence into a structured framework for medical decision-making. Nearly three decades later, EBM has transformed clinical practice but faces persistent challenges: limited generalizability of randomized controlled trials (RCTs), the dominance of statistical over clinical significance, and difficulties translating population-level findings to individual patients.[2–4]

At the same time, the exponential growth of biomedical data from electronic health records (EHRs), digital devices, omics technologies, and imaging archives has both exposed and expanded the boundaries of traditional EBM.[5–7] This convergence of EBM's structural constraints with the data revolution has catalyzed the rise of data science and artificial intelligence (AI) as new analytical tools to synthesize information and generate actionable insights.[8] These technologies do not replace EBM; rather, they extend its reach while inheriting its structural and epistemic limitations.

Recent reviews have addressed AI in healthcare from technical, ethical, or regulatory perspectives, including algorithmic bias,[9] real-world data infrastructures,[10] large language models,[11] surveillance systems,[12] and governance frameworks[13] (see Table 1). However, these discussions often remain conceptually fragmented and do not fully situate AI within the epistemological and methodological foundations of EBM.

This review examines how AI is beginning to reshape the production, validation, and application of medical evidence, and how its impact depends on the structural conditions under which data are generated and governed. In the Americas, this debate is

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Reference	Primary scope and focus	Relation to EBM framework	Added value of present review
Chinta et al. (2024)	Algorithmic bias, fairness and mitigating strategies in ML	Views bias as a technical artifact and discusses its ethical implications.	Our review positions bias not just as a technical flaw, but as an inherited epistemic limitation of traditional EBM that requires structural rather than just algorithmic reform
Lin et al. (2026)	Methodological comparison of RWD platforms	Emphasizes the use of large-scale observational databases to complement RCTs	Our review moves beyond database descriptions to conceptualize Target Trial Emulation (TTE) and Digital Twins as the necessary evolution to solve EBM's generalizability crisis
Mansoor et al. (2025)	Systematic review of medical reasoning architectures in LLMs	Focuses on the "computational thinking" that mimics clinical reasoning	Our review integrates these technical capabilities into a temporal state-of-the-art framework, evaluating how AI changes the "supervisor" role of the physician within the EBM ecosystem
Goktas et al. (2025)	Multidisciplinary framework for trustworthy AI	Aligns AI deployment with global policy and Sustainable Development Goals	Our review argues that transparency is not enough: AI's clinical impact depends on redesigning evidence governance and incentives, and on ensuring methodological rigor, real-world implementation, and ongoing monitoring.
Mendes et al. (2025)	Narrative review of AI applications in public health surveillance and outbreak management	Focuses on real-time analysis of communicable diseases and internet-based data. Emphasizes population-level monitoring and early detection	Our review expand discussion by focusing on individualized evidence generation and the methodological reconfiguration of clinical research beyond epidemic surveillance

AI: Artificial intelligence, EBM: Evidence based medicine, LLMs: Large Language Models, ML: Machine Learning, RCT: Randomized control trials, RWD: Real world data, TTE: Target Trial Emulation.

Table 1: **Positioning of the present review in relation to prior reviews on AI in healthcare.**

particularly urgent. Persistent health-system segmentation and fragmentation shape unequal access to care and digital infrastructures.[14] The integration of AI into EBM therefore cannot be understood independently of the region's heterogeneous institutional and regulatory environments.

Search strategy and selection criteria

We followed the state-of-the-art (SotA) review methodology proposed by Barry and colleagues,[15] to explore how AI is reshaping the methodological, technological, and ethical boundaries of EBM. This approach emphasizes conceptual synthesis, critical evaluation, and integration of insights across disciplines. To structure the review, we adopted a temporal framework: *"where we are now," "how we got here," and "where we should go next."*[16]

References for this review were identified through a structured search of PubMed and Scopus for articles published between January 2000 and February 2026. The search terms included a combination of MeSH and free-text keywords such as "evidence-based medicine", "artificial intelligence", "machine learning", "deep learning", "natural language processing", "clinical decision support systems", "causal inference", "big data", and "precision medicine".

To capture emerging concepts and frameworks, we supplemented the search with grey literature from the World Health Organization, the U.S. Food and Drug Administration and the European Commission, as well as preprints from GreyGuide International, medRxiv and arXiv. Manual searches of reference lists from key articles were performed to identify additional sources.

The initial search yielded approximately 7700 records. Given the conceptual nature of this SotA review, we applied a tiered screening process to manage this volume. Titles and abstracts were screened for conceptual alignment with the methodological evolution of EBM, and approximately 150 articles were retained for full-text review based on their potential to contribute to the theoretical framework. Screening was conducted by DHA, MCGA and FOO through iterative consensus discussion.

Studies were included if they contributed through methodological innovation, empirical illustration, or critical discussion relevant to the integration of AI into evidence generation in healthcare. In total, 73 sources focusing on AI methodologies and clinical applications informed the conceptual synthesis, along with 33 references that provided historical and epidemiological foundations of EBM (see Appendix p.1). Given the conceptual nature of this SotA review, studies were not weighted quantitatively. The aim was not exhaustive coverage but rather a critical synthesis of influential and emerging perspectives in the field.

Results

From experience-based to evidence-based medicine

Origins and methodological principles

The principles underpinning Evidence-Based Medicine (EBM) emerged long before the term itself. Early examples, from James Lind's scurvy experiment in 1747 to John Snow's spatial analysis of cholera, illustrate efforts to discipline medical intuition through systematic observation and quantification.[17–20] Throughout the nineteenth and early twentieth centuries, figures such as Florence Nightingale, Pierre Louis, and Ignaz Semmelweis demonstrated that empirical data could challenge prevailing clinical dogma and reduce harm.[21,22]

By the 1980s, EBM began to take shape as a formal movement. David M. Eddy introduced the term

"evidence-based" in relation to clinical guidelines, advocating decisions grounded in explicit evidence rather than tradition or expert opinion.[23] Alvan Feinstein, David Eddy, Gordon Guyatt, Archie Cochrane, and David Sackett transformed these principles into a structured discipline that integrated clinical expertise, patient values, and rigorous evidence appraisal.[22,24–26] David Sackett further advanced the field by promoting the teaching of clinical epidemiology, embedding critical evaluation skills into medical training and refining EBM into a structured, reproducible framework.[1,27]

EBM emerged as a methodological response to uncertainty, bias, and variability in clinical judgement. The turn towards AI is motivated by similar concerns: to extend the scope of inference and reduce subjectivity. Yet, as we argue, AI inherits many of EBM's unresolved challenges.

Why EBM alone cannot sustain modern medicine

As EBM became mainstream, methods for implementing and evaluating evidence grew more sophisticated. Frameworks such as GRADE formalized how to assess the quality of evidence and the strength of recommendations,[28] while systematic reviews and meta-analyses became central to guideline development and practice.[29] Despite these advances, EBM's practical implementation continues to reveal limitations that are as much structural as methodological.

Randomized controlled trials (RCTs), while central to causal inference, are costly, narrowly selective, and often conducted under idealized conditions that limit their external validity.[30–34] The dominance of p values over clinical relevance, along with publication and funding biases, has narrowed research agendas to questions that are commercially attractive rather than clinically pressing. Industry sponsorship shapes study design and reporting, leaving many high-impact but low-profit questions unexplored.[35]

These constraints arise not only from methodological design but from entrenched academic and economic hierarchies that define what counts as evidence. If these hierarchies persist in the AI era, algorithmic systems may amplify rather than correct longstanding inequities in knowledge production.[2,36–39]

Taken together, these limitations suggest that the classical tools of epidemiology and biostatistics remain indispensable but insufficient to address the scale, heterogeneity, and immediacy of contemporary health challenges.[37,40]

When prediction meets causation: data science and epidemiology in dialogue

Epidemiology and biostatistics are the foundational disciplines of health sciences.[41] Epidemiology seeks to explain the distribution and determinants of disease through causal inference and interpretability,[42] while biostatistics supplies the mathematical tools to design studies, control bias, and quantify uncertainty.[42] Together, they have sustained EBM by embedding methodological rigor into the generation of clinically meaningful knowledge.[43]

The exponential growth of biomedical data, from electronic health records (EHRs) and imaging repositories to multi-omics platforms, has exposed the limits of these classical tools and urged the rise of data science and AI.[40,44,45] Data science has emerged as a complementary paradigm. Whereas classical epidemiology prioritizes explanatory models and causal mechanisms, machine learning often optimizes predictive accuracy without explicit identification assumptions or guarantees of causal validity.[46] The epistemic distinctions between predictive, causal, and prescriptive approaches are summarized in Table 2.

Merging epidemiology's causal discipline with data science's computational power can yield models that are both interpretable and actionable, capable of guiding individualized care while informing population-level policy.[8,47,48] When used in concert rather than competition, these paradigms strengthen the evidentiary core of medicine and prepare the ground for AI-supported clinical reasoning.

Rethinking clinical trials: the promise and blind spots of emulated designs

New frameworks have emerged to bridge the internal validity of RCTs with the external generalizability of real-world evidence (RWE). Emulated clinical trials (ECTs) seek to reproduce key elements of RCTs, eligibility criteria, exposure assignment, outcome definitions, and analytic strategies, within large real-world datasets such as EHRs and insurance claims.[49] When traditional trials are infeasible because of ethical, economic, or logistical constraints, ECTs offer a pragmatic alternative.[49,50]

To enable such approaches at scale, while preserving rigor and reproducibility across heterogeneous sources, observational evidence generation increasingly relies on common data models (CDMs) and distributed research networks. Within this framework, OHDSI (Observational Health Data Sciences and Informatics), which uses the OMOP (Observational Medical Outcomes Partnership) common data model, standardizes heterogeneous sources and enables the execution of open, shared protocols across multiple data partners, facilitating replication, assessment of heterogeneity, and dynamic evidence updating.[51] These workflows incorporate epidemiologic design principles such as prespecified protocols and confounding adjustment, enabling reproducible observational evidence generation across heterogeneous data sources.[52] The LEGEND (Large-scale Evidence Generation and Evaluation across a Network of Databases) framework formalizes this approach for high-throughput comparative effectiveness and safety research, mitigating selective reporting.[53]

	Predictive ML	Causal inference	Prescriptive/Optimization
Epistemic aim	Risk estimation of future outcomes	Causal effect estimation and comparative effects	**Decision and policy optimization** under constraints
Question	"How likely is X?"	"What is the effect of A vs. B on outcome Y?"	"Which option is best in this context?"
Output	Probability or risk score	Treatment effect estimates and counterfactual contrast	Recommended action, policy or decision strategy
Role in EBM	Prognostic evidence for clinical stratification	Comparative effectiveness evidence for treatment decisions	Translation of evidence into clinical and policy decisions
Typical data requirements	Labeled data with stable outcome definitions and representative variables	Clearly defined treatment, time zero, eligibility criteria, and measured confounders	Causal or structural model, defined objectives, constraints, and outcome data
Failure modes	Dataset shift, subgroup bias	Unmeasured confounding, selection bias, model misspecification	Policy instability, objective misspecification, distribution shift
Validation focus	External and temporal, calibration, **subgroup performance**, model monitoring and interpretability	Assessment of identification assumptions, sensitivity analyses, robustness to unmeasured confounding	Simulation and off-policy evaluation, prospective or pragmatic validation
Clinical applications	- Early diagnosis and disease risk prediction[8] - Operational risk prediction[47]	- Comparative drug effectiveness and safety evaluation[48] - Clinical and policy interventions evaluation[49]	- Care prioritization and resource allocation[50] - Individualized treatment recommendation[51]

Table 2: **Conceptual distinctions between predictive machine learning, causal inference, and prescriptive/optimization approaches in clinical evidence generation and decision-making.**

ECTs have been used for drug repurposing, comparative effectiveness research, and long-term safety surveillance.[50,54] The RCT-DUPLICATE project, for instance, replicated ten cardiovascular trials using real-world data and found that eight produced hazard ratios consistent with the original RCTs.[55] Lee and colleagues introduced STEDR, a deep-learning framework that emulates large-scale trials and estimates heterogeneous treatment effects across patient subgroups.[56] When based on rigorous design and fit-for-purpose datasets, ECTs can provide an avenue to evaluate interventions in underrepresented or previously excluded populations, partially addressing a long-standing equity gap in evidence generation.[3,4,57]

However, better data does not necessarily mean complete data. Artificial intelligence and advanced analytics can enhance data linkage and causal modeling, but they cannot compensate for the structural inequities that determine who generates, contributes to, and benefits from medical data. Structural disparities in access to care and digital infrastructure shape who is represented in real-world datasets, rendering certain populations systematically invisible and creating blind spots that may propagate bias across both classical and emulated frameworks. This limitation is particularly salient in parts of Latin America and the Caribbean, where fragmented information systems and uneven interoperability across public and private sectors constrain representativeness and linkage capacity.[58] In such contexts, emulated trials may amplify structural gaps unless representativeness and data linkage capacity are explicitly addressed. Discrepancies between RCTs and TTE should therefore be interpreted as reflections of contextual variation and data limitations rather than simple validation or invalidation of either method.

Extending, not replacing, classical methodologies: the role of artificial intelligence

The rise of AI in medicine reflects not a rupture but an expansion of the analytic frameworks that have long supported evidence-based reasoning. Classical biomedical research, grounded in hypothesis-driven design and inferential statistics, offered essential tools for validating interventions but struggled to capture the complexity and heterogeneity of real-world health data.[59,60] AI-supported medicine builds on these traditions by extending their analytic reach, from description and prediction toward simulation and prescription, while demanding renewed attention to ethical oversight and transparency (Fig. 1).[61]

Machine learning (ML) and deep learning (DL) methods introduce flexible, data-adaptive approaches capable of processing high-dimensional and unstructured information such as medical images, omics data, and free-text clinical notes. This flexibility, however, creates new vulnerabilities. Real-world data, particularly in EHRs, exhibit systematic missingness, miscoding, and documentation artefacts that can propagate bias and compromise validity.[62] Even advanced methods such as double machine learning improve efficiency without resolving the deeper problem of causal identifiability.[63–65]

While algorithms can uncover associations and generate hypotheses,[66,67] causal inference still depends on explicit assumptions and domain expertise that machine learning cannot automate.[68] Causal discovery remains experimental, and hybrid approaches show promise[69,70] but causal claims are context bound.

Bridging the gap between predictive accuracy and demonstrated clinical benefit remains a central barrier to implementation.[71] High algorithmic performance

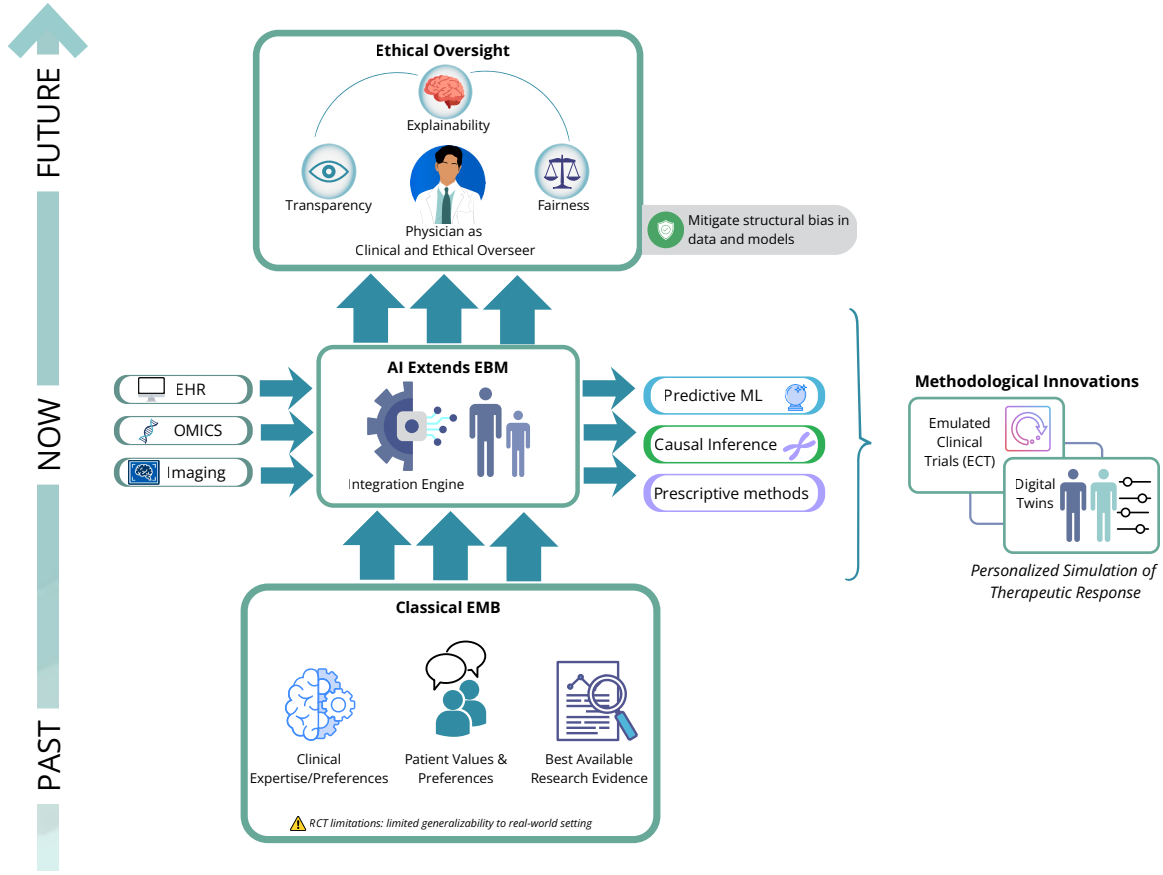

Fig. 1: **Artificial intelligence within the extended architecture of evidence-based medicine.** Conceptual map *illustrating* the evolution from classical evidence-based medicine to data science and AI-enabled evidence generation, framed within an explicit governance and ethics layer. The figure emphasizes that AI functions as an integrative analytic layer rather than a replacement for established methodological foundations. The figure was conceptually developed by the authors; an AI-assisted tool was used during early drafting to explore layout and structure, and the final version was fully redesigned and produced manually by the authors.

does not guarantee improved outcomes, safety, or fairness in practice (see Table 2). Traditionally, efforts to ensure trustworthy deployment have emphasized interpretability, rigorous external validation, and human-in-the-loop governance to ensure justifiable decisions and bias control.[65,72]

Implementation science offers a rigorous pathway to move AI from prototypes to sustained use in clinical practice. Evaluation should go beyond performance and interpretability and include post-deployment monitoring of performance, safety, and equity, with recalibration as patient populations, workflows, or standards of care change. Frameworks such as CFIR (Consolidated Framework for Implementation Research)[73] and RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance)[74] emphasize that successful AI adoption depends on context, intervention design, and the implementation process, thus requiring pragmatic and hybrid studies that assess both clinical and implementation outcomes. Complementarily, TRIPOD + AI (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis—Artificial Intelligence)[75] highlights the importance of transparency and rigorous external validation to ensure safe and reproducible deployment. Initiatives such as CONSORT-AI (Consolidated Standards of Reporting Trials—Artificial Intelligence)[76] and SPIRIT-AI (Standard Protocol Items: Recommendations for Interventional Trials—Artificial Intelligence)[77] reinforce these trial and reporting standards. Together, these approaches strengthen the evidence base for the clinical translation of AI, while interpretability is no longer viewed as the sole central safeguard.

Post-hoc interpretability techniques such as saliency maps, heatmaps, or SHAP values often provide limited guarantees of validity and may obscure reliance on shortcut features or spurious correlates.[62,78] Trustworthy deployment depends less on explanatory visualizations than on rigorous error auditing, subgroup analysis, and continuous monitoring.

From prediction to simulation: emerging roles of AI in evidence generation

AI is beginning to reshape how medical evidence is generated and applied. In critical care, ML models predict sepsis outcomes by integrating dynamic variables such as urine output and organ dysfunction scores, enabling earlier intervention.[79] In neurology, DL applied to MRI detects prodromal Alzheimer's disease, generating risk maps that can guide surveillance.[80] In oncology, multi-omics models integrate genomic and transcriptomic profiles to anticipate responses to immunotherapy, advancing precision medicine.[81] Collectively, these examples show how AI can extend clinical reasoning from population averages towards more individualized prediction and adaptive management.

Methodologically, AI alters the architecture of evidence generation. Predictive models move beyond assumptions of linearity and independence, capturing high-dimensional, non-linear interactions. Prescriptive models go further, using optimization algorithms to recommend interventions that balance clinical, economic, and logistical constraints.[72] Hybrid systems such as Mandava et al.'s DL framework for cardiovascular risk or Divyashree et al.'s web-based clinical decision support system (CDSS) demonstrates how automated feature extraction can reduce human bias and link inference directly to action.[82,83]

Simulation and implementation: from virtual models to real-world systems

Beyond prediction, AI facilitates simulation. In computational physiology, AI-enhanced Navier–Stokes models generate patient-specific simulations of cardiovascular hemodynamics, bridging classical fluid dynamics with individualized modeling.[84–86] Digital twins, dynamic, data-driven virtual replicas of patients, extend this logic further. By integrating longitudinal and multimodal data, they emulate disease trajectories and therapeutic responses, providing a *hypothetical* framework for exploring individualized causal effects under idealized data conditions.[87,88] Applications such as Pandey et al.'s oncology twin ecosystem or Li et al.'s graph-based multi-omics model for drug response prediction illustrate how these simulations may support experimentation when grounded in sufficiently rich and representative datasets.[89,90] Yet these capabilities remain aspirational for most real-world settings, as their validity depends entirely on the nature, completeness, and equity of the data that feed them.

However, the current enthusiasm around digital twins must be tempered by their structural limitations. Most clinical datasets do not capture all the relevant features that define a patient's true physiological or social state, disease severity, environmental exposures, behavioral factors, social determinants, or treatment nuances.[62,88] Moreover, data collection intensity varies widely across patients, meaning that two individuals may appear "digitally identical" while being clinically very different due to uncaptured variables.[44] Digital twins therefore achieve their highest fidelity only in well-represented populations and risk becoming dangerously misleading for under-represented groups.[91] As long as the social patterning of data generation remains unaddressed, digital twins cannot be assumed to advance evidence-based medicine and should instead be viewed as experimental tools whose validity depends entirely on the completeness, equity, and provenance of the underlying data.[62,91]

The expansion of AI into routine practice further illustrates how research methodologies are evolving into real-time analytics. Multimodal triage algorithms,[92] natural-language-processing chatbots that convert patient narratives into structured data,[93] and adaptive dosing systems for erythropoietin therapy illustrate the migration from static regression models to dynamic, learning control systems.[94]

Yet real-world deployments such as China's "Brilliant Doctor" CDSS reveal persistent human-machine misalignments, limited usability, interoperability gaps, and workflow friction, emphasizing that effectiveness depends as much on sociotechnical design as on algorithmic sophistication.[95]

AI systems do not operate as isolated predictive engines but are embedded within clinical informatics infrastructures; their effectiveness depends not only on predictive performance but on integration into clearly defined clinical workflows. When outputs are misaligned with practice realities, even high-performing systems can increase cognitive burden, undermine adoption, or generate implementation failure.[96] Moreover, algorithmic systems may induce automation bias or, conversely, algorithm aversion, highlighting that explainability alone does not guarantee meaningful oversight. Trust also requires calibrated communication of uncertainty, institutional accountability, and clinicians' ability to contextualize and contest recommendations.[97] Effective human–machine collaboration therefore depends on sociotechnical architectures that align algorithmic outputs with clinical reasoning while preserving clinicians as accountable supervisors within an AI-supported EBM framework.

Taken together, these developments indicate that AI-supported medicine is less a collection of new tools than a reconfiguration of research methodology itself. By automating feature discovery, synthesizing multimodal data, generating synthetic cohorts, and optimizing interventions, AI expands the statistical and epidemiological toolkit into a paradigm of *continuous evidence generation*. Its responsible adoption, however, requires rigorous validation, transparent governance, and equitable implementation to ensure that methodological innovation translates into ethically sound and clinically meaningful improvements in patient

outcomes.[98] Crucially, these safeguards cannot be achieved through technical refinement alone. The transformative potential of AI in evidence-based medicine depends on the redesign of governance structures, incentive systems, and sociotechnical environments in which algorithms operate. Absent such structural change, AI will more likely reinforce existing hierarchies of knowledge and access than correct them.

When openness is not enough: the shared limits of open science and artificial intelligence

The Open Science (OS) movement has gained global traction as a strategy to enhance transparency, reproducibility, and collaboration in research. In principle, OS strengthens EBM by democratizing access to the data and publications that form its evidentiary base.[38,39] Within global health, it has been heralded as a pathway to equity, an effort exemplified by UNESCO's initiatives to promote universal access to scientific knowledge.[99]

Yet this narrative obscures how OS operates within unequal hierarchies. Practices largely designed in the Global North may inadvertently reinforce existing inequities, particularly in the Americas, where research funding and analytic capacity remain unevenly distributed between North America and Latin American countries.[100–102] In this context, unrestricted data sharing can enable extractive practices such as "helicopter research," in which data are sourced from low- and middle-income countries without equitable participation in analysis or authorship. These dynamics reveal a deeper problem of epistemic injustice: the authority to define which knowledge counts and whose priorities matter remains unequally distributed.[102]

The challenges facing AI in medicine are structurally analogous. Just as scientific research has historically relied disproportionately on data from high-income countries, AI systems trained primarily on these datasets risk exporting biased or ineffective models to underrepresented populations.[103] Framing either OS or AI as neutral technical reforms overlooks their nature as sociotechnical systems embedded within existing power asymmetries.[104] Without explicit attention to governance, capacity building, and equitable participation, both may reproduce rather than mitigate inequities in knowledge production and healthcare delivery.

AI will not transform EBM without structural change

AI's promise to transform EBM cannot be taken at face value without asking under what conditions evidence is produced, governed, and monetized. Contemporary health data infrastructures are organized around extraction and control: institutions and companies collect and commercialize data from populations who have little control over how their information is interpreted or redeployed, while the corporatization of healthcare and the concentration of digital infrastructures in a few platforms create a highly asymmetric situation in which access to data, compute, and models is mediated by actors accountable primarily to investors.

Across the Americas, regulatory and institutional capacities for AI governance evolve unevenly.[105] In the absence of coordinated regional strategies, AI deployment risks widening divides between highly digitized tertiary centers and under-resourced public systems. Academic incentive structures and funding priorities also shape which research questions are pursued, which outcomes are valued, and which populations become statistically visible as "evidence."

Recent analyses of open science in global health demonstrate that openness alone does not redistribute epistemic power or advance equity; rather, governance must address who benefits, who participates, and who has the capacity to use shared resources.[91] By analogy, AI-enabled EBM requires not only methodological innovation but governance arrangements that redistribute analytic capacity, strengthen regulatory oversight, and ensure accountability for how algorithms influence clinical priorities and resource allocation.

Our claim is therefore not that AI will transform EBM on its own. Rather, AI can contribute constructively only within systems intentionally designed to promote transparency, fairness, and equitable infrastructure development. Without structural reform in data ownership, institutional accountability, and regulatory coordination, AI is more likely to optimize existing hierarchies than to correct them.

Conclusion

Medicine has continually evolved in how it produces and applies knowledge. What began as a discipline rooted in expert intuition matured into EBM, where clinical expertise, patient values, and empirical data converged to guide decisions. Today, AI represents not a rupture but an extension of this trajectory.

Rather than a rupture, AI represents the integration of epidemiologic reasoning, statistical rigor, and computational capacity. It preserves the core principles of systematic observation, critical appraisal, and reproducibility while broadening their reach through multimodal data integration, longitudinal real-world evidence, emulated trials, and simulation-based approaches. In doing so, AI offers new tools to narrow the persistent gap between population-level findings and individualized clinical decisions.

Yet analytic sophistication does not guarantee causal validity or equitable impact. Responsible adoption requires rigorous design, transparent validation, and sustained attention to data provenance and bias. Governance structures that ensure accountability and independence from commercial or institutional pressures remain essential to preserve the integrity of evidence generation. Clinicians must remain central—able to

interrogate, contextualize, and, when necessary, challenge algorithmic recommendations—so that technology strengthens rather than displaces clinical judgment.

The convergence of human and artificial intelligence redefines but does not diminish the physician's role. It positions clinicians as supervisors of complex digital systems and ethical stewards of data-driven medicine, responsible for upholding autonomy, beneficence, justice, and non-maleficence in an increasingly computational environment. The future of medicine will depend on this disciplined partnership: integrating human insight and machine precision with humility, transparency, and an unwavering commitment to equity.

Contributors

GACS: Conceptualization; Writing – Review & Editing; Resources; Supervision; Project Administration.

DHA: Conceptualization; Methodology; Investigation; Writing – Original Draft; Project Administration.

FOO: Conceptualization; Methodology; Investigation; Writing – Original Draft; Project Administration.

MCGA: Methodology; Writing – Review & Editing.

SAR: Methodology; Writing – Review & Editing.

FA: Conceptualization; Writing – Review & Editing.

SE: Conceptualization.

SJ: Writing – Review & Editing; Resources; Supervision.

LAC: Conceptualization; Writing – Review & Editing; Resources; Supervision.

All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

FOO and DHA directly accessed and verified the underlying data used in this study.

GACS had final responsibility for the decision to submit the manuscript for publication.

Data sharing statement

This Review did not involve the generation or analysis of any new datasets. All data referenced are from publicly available sources, including peer-reviewed literature and publicly accessible grey literature repositories.

Declaration of interests

We declare no competing interests.

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Appendix A. Supplementary data

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